

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-41 (**cancelled**)

42. **(New)** A method for generating at least one non-naturally occurring variant protein with at least one desired characteristic relative to a target protein comprising:

- a) inputting the coordinates of said target protein into a computer;
- b) identifying a list of variable residue positions in said target protein;
- c) applying at least one scoring function to said variable residue positions and said coordinates to generate a primary library comprising optimized variant protein sequences;
- d) identifying a set of amino acids at each of said variable residue positions in said variant protein sequences of said primary library;
- e) combining a first amino acid at a first variable residue position with at least a second amino acid at a second variable residue position, wherein said combining generates a secondary library of variant protein sequences; and
- f) screening said secondary library to identify at least one non-naturally occurring variant protein with said desired characteristic.

43. **(New)** A method according to claim 42 wherein said combining comprises:

- i) generating a set of oligonucleotide probes each encoding at least one of said variant amino acid residues;
- ii) using said probes in a polymerase chain reaction (PCR) to generate a plurality of oligonucleotide sequences, each encoding at least one of said second set of variant sequences; and,
- iii) producing said secondary library in host cells transformed with said oligonucleotide sequences.

44. **(New)** A method according to claim 42, wherein said scoring function is selected from the group consisting of a van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

45. **(New)** A method according to claim 42 wherein said step c) comprises a plurality of scoring functions.

46. **(New)** A method according to claim 42 wherein said step c) utilizes Protein Design Automation to computationally generate said optimized primary variant sequences.

47. **(New)** A method according to claim 42 wherein said generating of said primary variant positions is by using a probability distribution table.

48. **(New)** A method according to claim 42 wherein said combining of said primary variant positions is by using a probability distribution table.

49. **(New)** A method according to claim 42 wherein said combining is done computationally.

50. **(New)** A method according to claim 42 wherein said combining is done by using gene shuffling.

51. **(New)** A method according to claim 42 wherein said combining is done by using multiple PCR with pooled oligonucleotides.